REMARKS

Claims 1-33 were pending in this application. Claims 6, 18-24, 26-27 and 29-33 are canceled as drawn to non-elected Groups. Applicants expressly reserve the right to pursue protection of any or all of the subject matter of the canceled claims in a subsequent application. Claims 1, 2, 7, 8, 10, 17, and 28 have been amended and claims 34-37 have been added. Support for these claim amendments and new claims is discussed below where necessary.

Two paragraphs on page 10 of the specification have been amended to correct obvious clerical errors. A third paragraph on page 15 has been amended to add cell depository identifiers corresponding to the originally described cell line designations. As directed by the Examiner, information sheets from the applicable cell line depositories, which show both the cell line designation (*i.e.*, common name) and the corresponding cell line depository identifier, are attached as Exhibit A.

No new matter is introduced by these amendments. After entry of this amendment **claims 1-5, 7-17, 25, 28, and 34-37 are pending in this application**. Consideration of the pending claims is requested.

Telephone Interview

Applicants thank Examiners Belyavskyi and Chan for the courtesy of a telephone interview with their representatives Sheree Lynn Rybak, Ph.D., and Debra A. Gordon, Ph.D. on August 18, 2003. During the telephone conference, the rejections under 35 U.S.C. §112, first and second paragraphs were discussed.

The examiners indicated that a claim identifying the characteristics of the glioblastoma culture supernatant factor(s), such as in original claim 18 (canceled herein as drawn to a non-elected composition), or in the specification at page 17, Table II or at page 6, lines 5-25, would be sufficient to overcome the §112, first paragraph rejection that "[t]he specification does not enable . . . *any factor*. . . ."

Applicants requested clarification regarding the relevance of the Zou *et al.* reference (J. Immunol., 162:4882-4892, 1999), which was cited in the Office action (at page 6, paragraph 2). Based on a statement on page 4889 (first full paragraph, last sentence) of Zou *et*

al., the Office action alleged that the claimed factors "can be produced by some but not all glioblastoma cells." On this basis, the Office action concluded that "[t]he specification does not enable . . . *any glioblastoma cell.* . . ."

Applicants pointed out that the cited statement read that "some but not all cell lines from *other [non-glioblastoma] types of tumors"* (emphasis added) were not thought to produce immunosuppressive factors. That is, *non-glioblastoma* tumor cells do not produce factors that have the characteristics described by Applicants. On the other hand, glioblastoma culture supernatant (GCS) produced by both of the glioblastoma cell lines (*i.e.*, SNB-19 and U251) examined by Zou *et al.* exhibited immunosuppressive activity (see, *e.g.*, Zou *et al.*, page 4883, column 1, last line through column 2, first line; and page 4885, column 1, first full paragraph ending in column 2).

In addition, the Examiner suggested in the telephone interview that because SNB-19 did not produce IL-10 in the Zou *et al.* study (see, page 4889, second full paragraph, second sentence), then SNB-19 did not produce immunosuppressive factor(s). Applicants pointed out that Zou *et al.* exposed monocytes to GCS produced by SNB-19, and measured IL-10 expression *by the monocytes* as an indicator of GCS immunosuppressive activity (see, *e.g.*, Zou et al., at page 4884, column 2, "Effect of GCS on cytokine production"). An increase in IL-10 production *by GCS-exposed monocytes* was proposed to be one element of cytokine dysregulation in monocytes, which subsequently led to T cell immunosuppression (see, *e.g.*, Zou *et al.*, page 4889, column 1). Thus, the fact that SNB-19 cells did not produce IL-10 in the Zou *et al.* study is not relevant to the contention in the Office action that only some glioblastoma cells produce the factors described by Applicants. IL-10 expression by monocytes is merely useful as an indicator that GCS produced by SNB-19 in fact contains the claimed factors. Therefore, Zou *et al.*, does not support the enablement rejection as formulated in the Office action.

In light of the discussion of the Zou *et al.* reference, the examiners agreed to consider Applicants written arguments about the cited references.

The examiners questioned whether the cell lines described in the specification were created by the Applicants. Applicants' representatives explained that the cell lines were not created by Applicants (see, *e.g.*, page 22, lines 2-9) and that each of the claimed cell lines is commercially available and/or readily known in the literature. The Examiners agreed that cell lines available from commercial cell line depositories located, at least, in the United States

(*i.e.*, American Type Culture Collection, aka ATCC, P.O.Box 1549, Manassas, VA 20108) and Europe (*e.g.*, Deutsche Sammlung von Mikroorganismen und Zellkulturen, aka DSMZ, Mascheroder Weg 1b, 38124 Braunschweig, Germany, and the European Collection of Cell Cultures, aka ECACC, United Kingdom, +44 (0) 1980 612684, ecacc.technical@camr.org.uk) are known and readily available if there are no unreasonable restrictions on purchasing such cell lines. The examiners further explained that amending the specification to add cell line depository identifiers (*e.g.*, ATCC no., DSMZ no., or ECACC no.) for the cell lines originally described only by common name (*e.g.*, laboratory cell line designation) would not be new matter if documentation showing a correlation between the laboratory cell line designation and the cell line depository identifier was provided.

Applicants believe this Amendment reflects many of the helpful suggestions made by the examiners during the interview.

Restriction Requirement

Applicants note that the Office action has made the restriction requirement final. Accordingly, claims 6, 18-24, 26-27 and 29-33 are canceled as drawn to non-elected Groups. Claims 11-13, and 25, which contain non-elected species, remain in the application pending allowance of one or more generic claim(s) encompassing the claimed species.

Information Disclosure Statement ("IDS")

In the August 18, 2003 telephone interview, Applicants also discussed the references listed on the IDS that were not considered by the Examiner. Applicants' representatives explained that the "missing" information, which caused the Examiner not to consider the particular references, did not appear to be available and that Applicants had disclosed all the available information. Applicants' representatives requested that the Examiner check his database to see if he could obtain additional information relating to the non-considered references. Applicants' representatives further explained to the Examiner that the American Type Culture Collection (ATCC) cell line information sheets, which were submitted with the IDS, were printed from the ATCC website, and therefore no catalog publication date or page number was available.

As discussed in more detail below, cell line information sheets showing the cell line name and depository identifier number are enclosed herewith (see Exhibit A). These information sheets were also printed from the applicable cell line depository website. Therefore, Applicants also will not be able to provide a catalog publication date or page number for the enclosed information sheets.

Brief Description of the Figures

The specification has been amended to clarify that figure legends on page 10 should refer to "Figure 12" and "Figure 13." In view of these amendments, Applicants request that the objection be withdrawn.

***Claim Rejections under 35 U.S.C. §112, 2nd paragraph*:**

Claim 1 and its dependent claims 2-17 and 25 have been rejected under 35 U.S.C. §112, 2nd paragraph because claim 1 allegedly omits a "resolution step."

Claim 1 has been amended, in relevant part, to recite a step of "introducing a therapeutically effective amount of the APCs exposed to the immunosuppressive composition into a subject in whom a reduced immune response to the antigen is desired, wherein introduction of the APCs inhibits the immune response of the subject to the antigen." The foregoing step provides a "resolution step" that correlates the preamble with the first step of claim 1. This claim amendment is supported by the specification, *e.g.*, at page 18, lines 11-24, and at page 19, lines 8-13. In view of this amendment, Applicants request that the rejection be withdrawn.

Claim 17 has been rejected under 35 U.S.C. §112, 2nd paragraph because the cell line designations "SNB 19, U251[,] A172, A1207, A1235, A2781, U87 MG, U138 MG and U373 MG" are allegedly indefinite. Applicants traverse this rejection on the ground that those skilled in the art understand these designations, as evidenced by hundreds of journal abstracts on PubMed that refer to these designations. However to expedite prosecution of this application, claim 17 has been amended to add cell depository identifiers for SNB 19, A172, U87 MG, U138 MG, and U373 MG in accordance with the Examiner's suggestions,

The Office action (at page 4, first sentence) states that "[a]mending the claim to recite the appropriate ATCC Accession Number would obviate this rejection." Further, in the telephone interview, the Examiner agreed that other cell depository identifiers would be equally acceptable with evidence showing a correlation between the laboratory cell line designation and the cell line depository identifier was provided. The cell depository information sheets in Exhibit A show the correspondence between each claimed common cell line name and its respective cell depository designation.

The common cell line designations for U251, A172, A1207, and A1235 have been removed from claim 17, and are discussed below in connection with newly added claims 37 and 38.

In view of these amendments and the supporting information, Applicants request that this rejection be withdrawn.

Claim 28 has been rejected under 35 U.S.C. §112, 2nd paragraph as allegedly indefinite because it depends on non-elected claim 18. Claim 28 has been amended so that it does not depend from claim 18. Thus, the rejection is moot, and Applicants request that it be withdrawn.

***Claim Rejections under 35 U.S.C. §112, 1st paragraph*:**

Claim 17 has been rejected under 35 U.S.C. §112, 1st paragraph (enablement) because SNB 19, U251 A172, A1207, A1235, A2781, U87 MG, U138 MG and U373 MG are allegedly "required to practice the claimed invention . . . and must be known and readily available to the public or obtainable by a repeatable method set forth in the specification."

As discussed above, claim 17 has been amended to add cell depository identifiers for SNB 19, A172, U87 MG, U138 MG, and U373 MG, and to remove the U251, A172, A1207, and A1235 common cell line designations. In the telephone interview, it was made clear that the claimed cells were not created by Applicants. In fact, all of the cell lines recited in amended claim 17 are available from at least the one commercial source whose identifier is recited in the

claim, and most of the cell lines are also available from other recognized cell depositories, as indicated in the following table:

Cell Line Name	ATCC No.	DSMZ No.	ECACC No.	ICLC No.*
SNB-19		ACC 325		
A172	CRL-1620		88062428	HTL97013
U87 MG	HTB-14		89081402	HTL00013
U138 MG	HTB-16	ACC 291		
U373 MG			89081403	HTL99014

*Interlab Cell Line Collection, Istituto Nazionale per la Ricerca sul Cancro, L.go R. Benzi, 10, 16132 Genova, Italy

Applicants provide, as Exhibit B, publicly available information from each of the cell depositories whose identifiers are recited in amended claim 17 (*i.e.*, ATCC, DSMZ and ECACC) that shows the applicable cell lines are available upon payment and satisfaction of other commercially reasonable requirements.

Thus, the cell lines recited in amended claim 17 are known and are readily available without unreasonable restriction, and Applicants request that the rejection be withdrawn.

Claims 1-17, 25 and 28 have been rejected under 35 U.S.C. §112, 1st paragraph (enablement) because the specification allegedly does not provide enablement for "a method . . . comprising exposing purified or isolated APC to *any* factor secreted by *any* glioblastoma cell." Applicants traverse this rejection and request reconsideration.

As discussed in the telephone interview of August 18, 2003, the Examiner agreed that a claim identifying the characteristics of the glioblastoma culture supernatant factor(s), such as in original claim 18 (canceled herein), or in the specification at page 17, Table II or at page 6, lines 5-25, would be sufficient to overcome the rejection that "[t]he specification does not enable . . . *any factor*. . . ." Applicants have amended independent claims 1 and 28 (and, therefore, dependent claims 2-17 and 25) to recite characteristics of the factor(s) as described in original claim 18. In addition, dependent claims 2 and 34 now recite characteristics of the factors as described on page 6, lines 5-25 of the specification.

To support the rejection that "[t]he specification does not enable . . . *any glioblastoma cell*. . . ," the Office action contends that the Zou *et al.* reference teaches that the claimed factors "can be produced by some but not all glioblastoma cells." Zou *et al.* does not support the alleged teaching. Briefly, Zou *et al.* teaches that *non-glioblastoma* tumor cells do not produce factors that have the characteristics described by Applicants. In contrast, the two glioblastoma cell lines (*i.e.*, SNB-19 and U251) disclosed by Zou *et al.* did produce factors that induced an immunosuppressive response from APCs. Thus, Zou *et al.* can not support this §112, first paragraph rejection. Applicants further note that Zou *et al.* is not available as prior art in this case, as acknowledged by the Examiner in the telephone interview.

On the basis of the foregoing amendments and arguments, Applicants request that this rejection be withdrawn.

Claims 1-17, 25 and 28 have been rejected under 35 U.S.C. §112, 1st paragraph (written description) because the Applicants allegedly is not in possession of "a method . . . comprising exposing purified or isolated APC to *any* factor secreted by *any* glioblastoma cell." Applicants traverse this rejection and request reconsideration.

The Office action states (at page 7, paragraph 7) that the written description requirement is satisfied for "a method of specifically inhibiting an immune response to one or more selected antigens comprising exposing purified or isolated APC[s] to a specific factors (sic) disclosed in the specification on page 6, lines 5-25 and Table [II], page 17, that [are] secreted by SNB19, U251, A 172,A1207, A 1235, A 2781, U 87MG, U138 MG and U373MG cell lines." In the telephone interview, the Examiner also tentatively agreed that original claim 18 (canceled herein) recited a satisfactory description of the claimed factors.

As suggested by the Examiner, independent claims 1 and 28 (and therefore dependent claims 2-17 and 25) have been amended to recite factors having the physicochemical characteristics set forth in original claim 18. Moreover, amended claim 2 and new claim 34 recite factors having the physicochemical characteristics set forth in the specification on page 6,

lines 5-25. Thus, in keeping with the Examiner's suggestions, the "any factor" basis of this written description rejection is overcome.

With regard to the "any glioblastoma cell" basis for this rejection, amended claim 28 further recites each of the cell lines described in the original specification for which a cell depository designation is available. Thus, claim 28 recites a method that the Examiner has expressly stated satisfies the written description requirement, and Applicants request that this rejection of claim 28 be withdrawn.

Further regarding the "any glioblastoma cell" basis of this rejection, Applicants submit that amended claim 1 (and its dependent claims) also satisfies the written description requirement without a recitation of specific glioblastoma cells. As pointed out above, the Office action says that Applicants have provided sufficient written description for nine glioblastoma cell lines (*i.e.*, SNB19, U251, A 172,A1207, A 1235, A 2781, U 87MG, U138 MG and U373MG). Nine cell lines is a representative number of species that clearly shows possession of a genus of glioblastoma cells. In view of the foregoing amendments and arguments, Applicants request that this rejection of claim 1 and dependent claims 2-17 and 25 be withdrawn.

***Claim Rejections under 35 U.S.C. §102*:**

Claims 1, 3, 4, 6, 13-16 and 28 have been rejected under 35 U.S.C. §102(a) as being allegedly anticipated by Dix *et al.*, *FASEB J.*, 13(4):A610, 1999 ("Dix"). Applicants traverse this rejection and request reconsideration.

Attached to this Amendment as Exhibit C is a Declaration of Jian-Ping Zuo and Gene M. Shearer Under 37 C.F.R. §1.132 ("Declaration"). The Declaration states that the Applicants are among the authors of the Dix reference, and that the non-inventor authors of the Dix reference (*i.e.*, Dix, Morford, Brooks, and Roszman) learned or received knowledge about the invention (as described in the Dix reference) from the Applicants. Thus, the Dix reference describes the Applicants own work, and is not available as prior art under §102(a). Applicants request that the rejection be withdrawn.

Claims 1, 3, 4, 6, 13-16 and 26 have been rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Zou *et al.*, *J. Acquir. Immune Defic. Syndr. Hum. Retrovirol.*, 14:A30, 1997 ("Zou"). Applicants traverse this rejection and request reconsideration.

As discussed above, claim 1 (and its dependent claims 3, 4, and 14-16) has been amended to recite a step of "introducing a therapeutically effective amount of the APCs exposed to the immunosuppressive composition into a subject in whom a reduced immune response to the antigen is desired, wherein introduction of the APCs inhibits the immune response of the subject to the antigen." Zou does not teach nor suggest the foregoing step, and therefore cannot anticipate claim 1 (or its dependent claims). Claims 6 and 13 have been withdrawn, and claim 26 has been canceled. Thus, Applicants request that this rejection of claims 1, 3, 4, 6, 13-16 and 26 be withdrawn.

Newly Added Claims

Claim 34 is supported, at least, by original claim 19.

Claims 35 and 36 recite common cell lines names, which are supported at least by original claim 17. The recited cell lines are known. As summarized in the following table, each of the claimed cell lines is described by various different investigators in numerous publications listed in the PubMed database (accessible at the National Center for Biotechnology Information website under the "Literature databases" heading and "PubMed" link).

Cell Line Name	No. PubMed Hits Based On Search Of Cell Line Name
U251	314
A1207	9
A1235	15

As one of skill in the art would recognize, it is common practice in the scientific community to make cells lines (and other research tools) available upon request. Thus, the cell lines recited in claims 37 and 38 are readily available by simple request of one or more of the investigators who have published work involving the respective cell lines.

Because the U251, A1207, and A1235 cell lines are both known and readily available, it is believed that claims 37 and 38 satisfy 35 U.S.C. §112 and are otherwise allowable.

Claim 37 recites glioblastoma cells having ATCC nos. described in and supported by the original specification, for instance, at page 15, line 28 through page 16, line 1.

Other Claim Amendments

Claim 2 has been amended to recite characteristics of the factor(s) as described in original claim 19 (now canceled as drawn to a non-elected composition).

Claim 7 has been amended to change its dependency.

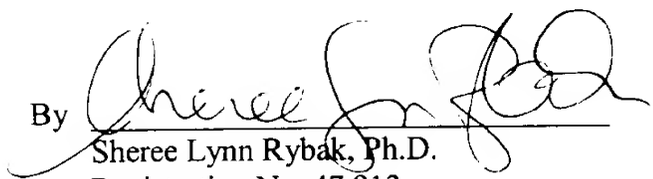
Claim 8, which depends from claim 1, has been amended to remove the phrase "a sufficient dose of," because that phrase is redundant in light of the claim 1 amendments.

Claim 10, which depends from claim 1, has been amended to remove the phrase "and the introducing step comprises administering a therapeutically effective amount of the exposed APCs to the subject," because that phrase is redundant in light of the claim 1 amendments.

It is respectfully submitted that the present claims are in condition for allowance. If it may further issuance of these claims, the Examiner is invited to call the undersigned at the telephone number listed below.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By 

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